

# Modelling the Health Economic Impact of Influenza Vaccination Strategies for High-Risk Children in Vietnam

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## ABSTRACT

**Introduction:** In Vietnam, since 2011 a National Influenza Surveillance System in Vietnam has implemented Severe Acute Respiratory Infection (SARI) surveillance to assemble information and inform administrative and methods of prevention. Children and elderly people belonging high risk-group are recommended for vaccination whereas, need for cost effectiveness study to aid strategic decisions on Vietnamese Expanded Program on Immunization.

**Aim:** To explore the cost-effectiveness analysis of influenza vaccination strategies for high-risk children in Vietnam.

**Materials and Methods:** The outcomes of influenza vaccination were calculated by cost-effectiveness analysis in children which were monitored until the age of 15-year-old. Cost-effectiveness analysis were performed based on Quality-Adjusted Life-Years

(QALYs) gained due to vaccination comparing to no vaccination. Country-specific data of Vietnam was approached as much as possible for input parameters. Cost-effectiveness analysis was performed in terms of Incremental Cost-Effectiveness Ratio (ICER), and cost benefit analysis is presented as net present value.

**Results:** Cost of get vaccination program was recorded at 30.68 USD (the United State Dollar), whereas cost of no get vaccination program was 17.99 USD. The ICER of get influenza vaccine versus no influenza vaccine in children under 15-year-old were USD 25.31 USD/QALY (quality-adjusted life-years) and 31.03 USD/QALY for social and healthcare provider perspective.

**Conclusion:** To better inform the policy decisions of influenza prevention and control to give influenza vaccination into Vietnamese Expanded Program on Immunisation (VEPI), economic and math models are necessary.

**Keywords:** Cost-effectiveness, QALY, Severe acute respiratory infection

## INTRODUCTION

Influenza, a respiratory illness often recognised with the common symptoms of fever and cough, is the cause of a yearly winter epidemic in almost 9% of the world population [1]. Vaccination undeniably has well-documented efficiency and other advantages, including few side effects and an affordable cost per dose of traditional vaccine. Nevertheless, influenza remains associated with sufficiently high statistics for influenza-associated morbidity and mortality to consider influenza cases as high risk [2,3]. A complementary approach for protecting the susceptible is indirect protection obtained by vaccinating others to reduce transmission of influenza. Vaccination of children has confirmed the potential to reduce morbidity and mortality in others [4].

The population of individuals housed in closed environments, such as nursing homes or military bases, show a disproportionate infection rate that could account for 40% of the total population [1]. Despite the accessibility of benign and effectual anti-influenza vaccines for children and the confirmed health and economic costs of influenza, the worldwide recommendations for childhood vaccinations vary considerably. In the northern hemisphere, vaccination is recommended for children over 6 months in the USA, Austria and Estonia [5-8]. A significant analysis and discussion on influenza vaccination cost-effective in children has been presented by various studies in Finland [9], Italy [10], Canada [11], the United States (US) [12] and Argentina [13]. Given the biological, clinical, epidemic and economic factors associated with vaccination programs, the estimation of cost-effectiveness usually requires a model [14]. However, the scarcity of material complicates the ability to develop comprehensive guidelines or frameworks that describe the best manner to execute Health Economic Evaluations (HEEs) of vaccines and incorporate the discoveries into the decision-making process for immunisation [15]. Hence, the policy effect of recurrent yearly vaccinations in several successive influenza seasons was

not considered in the models. As a result, the models could not incorporate the accumulated QALYs gained by the different age groups over a lifetime.

The present research explored, for the first time, the cost-effectiveness of influenza vaccination strategies for high-risk children in Vietnam. The overall aim was to characterise the numerous sources of complexity involved in estimating the economic impact of vaccination. Our hope was to provide researchers and policy-makers with new information and a better understanding of alternative methodological approaches, as they debated the implementation of expanded vaccination programs in VEPI.

## MATERIALS AND METHODS

### Study Design

**Scope of study:** This study applied decision-analytical modelling to analyse the cost effectiveness of influenza vaccination strategies for children under the age of 15 in Vietnam to help characterise the numerous sources of complexity in estimating the economic impact of vaccination.

**Decision-analytical model:** For cost-effectiveness analysis, a decision-analytical model in form of decision-tree model analysis was employed as a tool to produce the output values from the interventions. The output values were used to estimate the ICER. The total budget for Budget Impact Analysis (BIA) in this study was based on guidelines for estimating the costs of introducing new vaccines recommended by World Health Organisation (WHO) [16] into the national immunisation system.

**Time horizon and discounting rate:** Most costs and consequences related to influenza occur during a single influenza season; therefore, the time span of the model was one annual influenza season (January 2009-December 2009). Since the estimation of costs and outcomes was conducted during a one-year period, no discount rate were applied.

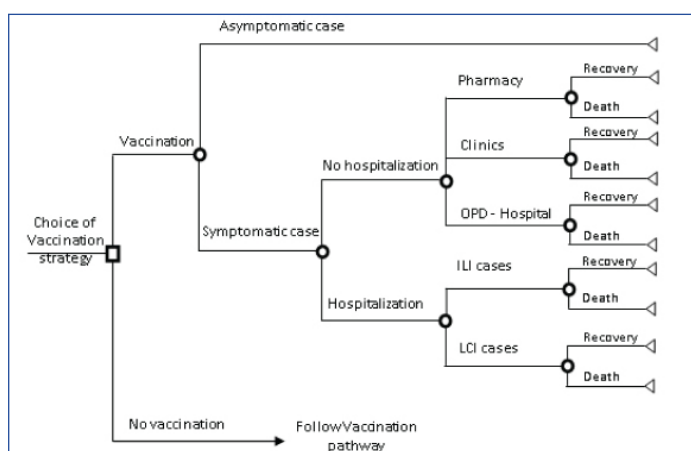
**Comparators:** The vaccination strategy in this study included participants with a vaccination program for influenza prevention (intervention) and without a vaccination program (no intervention).

## Model Design

In present study, the outcomes of influenza vaccination were calculated by cost-effectiveness analysis of children who were monitored until the age of 15 years [Table/Fig-1]. The model process was dichotomised by node with two possible options (such as with a vaccination program or no vaccination program). It operated on the basis of influenza infection and influenza-like illnesses (ILI). The model was analysed with Microsoft Excel 2010.

Cost-effectiveness analyses were performed based on QALY gained due to vaccination compared to no vaccination (treatment only), without other life quality elements, in children ranging from 0 to 15-year-old.

In the vaccination strategy branch, the coverage rate (97.2% in the base-case scenario) [17] decides the population of children receiving vaccine injections. However, not all vaccinated children are assured immunity from influenza, as the vaccine is not absolutely effective against the virus. Thus, a minority are likely to remain vulnerable to infection and will have a higher risk of contracting influenza. The subjects who receive vaccinations will probably also show a greater possibility of using medical services or having complications that may require special medical attention or even hospitalisation, since vaccination is assumed to be ineffective against the development of complications. By contrast, the unvaccinated children, despite their vulnerability to infection, which is associated with the attack rate, may not experience either minor or major complications under any circumstances.



**[Table/Fig-1]:** Decision diagram for vaccination versus no vaccination (treatment only).

## Model Input

Country-specific data [18] for Vietnam was utilised as much as possible for input parameters. International data sources [16] were used when input parameters could not be obtained from the Vietnam context. The values for all parameters, in sources such as vaccination records, health care costs, indirect costs and other relevant terms of the model, are described.

The next sections offer a closer and more elaborate look at the study conducted in particular regions of the population and housing census conducted in Vietnam during 2009 [19], with its main concentration on children under 15 years of age. Two age groups, with age limits of 0-4 and 5-15 years of age were studied.

[Table/Fig-2] demonstrates the base-case unit cost, probability, vaccination and utility data used in our model. The chosen standard unit of currency to display the value of all expenses in 2016 is USD [15,19-25].

**Influenza vaccination: efficacy, strain match, and overall effectiveness [20]:** An attempt to end the pandemic has never commenced since the vaccination program has not yet been put into motion; therefore, its efficiency is unknown. Separate analyses focusing on distinctive levels of vaccine effectiveness were chosen to be performed to allow for critical uncertainty in these main parameters. Moreover, because of the wide variation of efficacy of available vaccines against specific strains, the base vaccine efficacy was set at 60% since the vaccines show lower efficiency in elderly subjects [19]. The assumption is also made that the vaccine is similarly efficient in terms of reductions in illness, hospitalisation and mortality due to a scarcity of data that supports opposite viewpoints. The chosen parameters were considered, rather than separated stochastic variations, regarding its unreality (i.e., a low reduction in hospitalisation but a high reduction in case fatalities). Other key variables, such as a cross-creativity against the pandemic strain (strain mismatch) ranging from 0 to 100%, were not apparent in the vaccine. The difference between receiving vaccination and not receiving vaccination is labelled as the overall effectiveness; this relies on the proportion of influenza cases, which changes annually. Base-case estimates of the average distribution of influenza cases included influenza type A and influenza type B. The influenza clinical attack rate was calculated for 2009 from the epidemiologic data of National Influenza Surveillance System in Vietnam. The calculation made to evaluate the vaccine efficacy is as follows:

$$\text{Overall effectiveness (\%)} = \text{Vaccine efficacy (\%)} * (1 - \text{Strain mismatch (\%)})$$

**Costs:** In this study, two categories of costs are considered, including costs of vaccination and treatment costs of influenza, with two sub-categories of direct costs and indirect costs.

**Estimated costs of receiving a vaccination:** Vaccination costs have component factors that include direct medical costs (i.e., vaccine acquisition, administration, and adverse event costs), direct non-medical costs (i.e., transportation costs), and indirect costs based on expert opinions, which include the productivity loss associated with parents who take personal leave from work to care for their sick children, travelling costs for vaccine injection, meal costs and adverse events associated with the vaccines. The cost of the Trivalent Inactivated Influenza Vaccine (TIV) per dose used was 10.23 USD, based on the Hospital for Tropical Diseases price list; and the total costs for influenza was 26.18 USD, consisting of the injection service (1.17 USD), outpatient visit cost (4.57 USD) and indirect cost (9.67 USD) [19].

**Estimated treatment cost of influenza:** The influenza treatment costs consisted of costs of hospitalisation treatment and costs of non-hospitalisation treatment, such as the costs of treatment for patients at pharmacies, clinics and outpatient departments (OPD) at the hospital. Direct costs included direct medical costs (costs of emergency room admission, office visits, prescriptions and over-the-counter medications) and direct non-medical costs (costs of transportation, meals, accommodations and hiring of caregivers). The indirect costs consisted of cost that patients and caregivers lost due to absence at work and/or productivity loss. Due to the absence of agreements regarding the proper measurement applied to the costs, spending due to pain or mortality was excluded from this analysis.

\* Hospitalisation

ILI and Laboratory Polymerase Chain Reaction-Confirmed Test (LCI) were two groups included in the influenza-related hospitalisation treatment used to collect the costs in this study. Data for calculation of hospitalisation treatment costs in this study were taken from Vo TQ et al., [21]. Total hospitalisation costs per case included direct costs (76.27 USD for ILI cases, 254.49 USD for LCI cases), and indirect costs (62.40 USD for ILI cases, 208.22 USD for LCI cases)

Input data (Unit)	Mean	Standard Deviation or Range	Probability distribution	Source
<b>Treatment cost of influenza (USD)</b>				
<i>No Hospitalisation</i>				
<b>Pharmacy</b>				
Direct medical cost	5.29	6.12	Not varied	[22]
Direct non-medical cost	51.58	56.41	Not varied	[22]
Indirect cost	20.65	19.69	Not varied	[22]
Total cost	77.44	72.36	Not varied	[22]
<b>Clinics</b>				
Direct medical cost	19.72	40.29	Not varied	[22]
Direct non-medical cost	114.62	168.40	Not varied	[22]
Indirect cost	26.03	22.18	Not varied	[22]
Total cost	160.36	203.74	Not varied	[22]
<b>Hospital (OPD)</b>				[22]
Direct medical cost	25.13	14.41	Not varied	[22]
Direct non-medical cost	108.28	101.89	Not varied	[22]
Indirect cost	27.06	35.74	Not varied	[22]
Total cost	160.47	136.41	Not varied	[22]
<i>Hospitalization</i>				
<b>ILI cases</b>				
Direct cost	76.27	118.03	Not varied	[21]
Indirect cost	62.40	96.57	Not varied	[21]
Total cost	138.67	214.60	Not varied	[21]
<b>LCI cases</b>				
Direct cost	254.49	96.42	Not varied	[21]
Indirect cost	208.22	78.89	Not varied	[21]
Total cost	462.71	175.32	Not varied	[21]
<b>Probability</b>				
<i>Vaccine injection rate</i>	0.002	-	Not varied	Point estimated
<i>Vaccination ILI attack rate</i>	0.10	-	Gamma	[23]
<i>No Vaccination ILI attack rate</i>	0.16	-	Gamma	[23]
<i>No Hospitalisation</i>	0.91	-	Not varied	[24]
Pharmacy	0.64	-	Not varied	[15]
Clinical	0.27	-	Not varied	[15]
Hospital (OPD)	0.09	-	Not varied	[24]
<i>Hospitalisation</i>	0.09	-	Not varied	[24]
ILI cases	0.92	-	Not varied	[21]
LCI cases	0.08	-	Not varied	[21]
<i>Recovery rate</i>	1.00	-	Not varied	Point estimated
<i>Mortality (case fatality per 100000)</i>	5.00	-	Not varied	[20]
<b>Vaccination</b>				
Strain Mismatch	0.00	(0-100)	Not varied	Point estimated
Vaccine efficacy	0.60	-	Not varied	[20]
Overall Effectiveness	0.60	-	Not varied	[*]
<b>Costs for influenza vaccination (USD)</b>			Beta	
Influenza vaccine	10.23	-		(19)
Outpatient (OPD) service	4.57	-		[19]
Injection service	1.71	-	Not varied	[19]
Direct cost of vaccination	16.51	-	Not varied	[**]
Indirect cost	9.67	-	Not varied	Point estimated
Total cost of vaccination	26.18	-	Gamma	[***]
<b>Utility (QALYs)</b>			Not varied	
QALY loss	0.017		Gamma	[25]

[Table/Fig-2]: Input variables and costs used to calculate the economic impact of influenza-related events for a decision model [15,19-25].

Calculation

[\*] Overall effectiveness=Vaccine efficacy x (1-Strain match)

[\*\*] Direct cost of vaccination=Total cost (Influenza vaccine, Outpatient service, Injection service)

[\*\*\*] Total cost of vaccination=Total cost of (Influenza vaccine, Outpatient, Injection service, Caregiver)

[21].

\*No hospitalisation: Clinics, Pharmacy, OPD in hospital

One study by Vo TQ et al. [22] reported the social and economic burden of ILI and clinically diagnosed flu in patients treated at various health facilities in Vietnam. The total cost was the sum of indirect cost, direct medical cost and direct non-medical cost.

**Probabilities:** To estimate the proportion of outpatient visits, the rate of ILI treatment cases was recorded for the pharmacy (64%), clinic (27%) and OPD (9%). The proportion for inpatients in the hospital was 92% (ILI cases) and 8% (LCI cases) [22].

**Utility data:** In this study, due to the unavailability of utility data for children under 15 years of age who were asymptomatic cases and symptomatic cases, and due to time limitations, we computed an estimate of the QALY lost for each episode (QALY loss). The mean QALY loss per episode in children was 0.017.

**Analysis and presentation:** Cost-effectiveness analysis was performed in terms of the ICER, and cost benefit analysis is presented as the net present value [26].

### Sensitivity Analysis

The impact of uncertainty of the input data on the model results was assessed using one-way sensitivity analyses. Here, the parameter had a wide range of variation from its base-case value. The values of the data defined the ranges of the parameter used for the one-way sensitivity analyses, as well as the probable allocation for the probabilistic sensitivity analysis for the parameters with the highest impact on a cost-effectiveness threshold of 1 Gross Domestic Product (GDP) per capita per QALY lost.

To define the main parameters that had a variety ranging within  $\pm 10\%$ , sensitivity analyses were demonstrated for the involvement of influenza vaccination, attack rate and QALY lost due to influenza symptoms.

Probabilistic sensitivity analysis was performed in which input parameters were simultaneously varied according to their probability distributions. For each scenario, the model was run as a Monte Carlo simulation with 1,000 iterations to generate the ICER [27]. The input parameters included in the modelling were vaccine coverage, vaccine efficacy, vaccine and vaccination costs and the cost of the illness.

### Budget Impact Analysis

In this study, the total budget was estimated from the costs of vaccine supplies. The total vaccine costs per year, code as 'c', are estimated as " $c = p \times n$ ", where 'p' is price per dose of the new vaccine, including freight expenditures; and 'n' is number of doses supplied. For the first year, the number of doses supplied is estimated as " $n = i \times b \times d \times (1/(1-w)) \times (1+r)$ ", where 'i' is immunisation coverage rate; 'b' is birth cohort; 'd' is number of doses per Fully Immunised Child (FIC);

'w' is wastage rate (%); and 'r' is reserve stock (%). For subsequent years, the number of doses needed should be determined using the same formula, except that the reserve stock should be excluded and any vaccine in stock should be subtracted from the number of estimated doses, as follows: " $n = i \times b \times d \times (1/(1-w)) - s$ ", where 's' is the number of vaccine doses in stock.

## RESULTS

The estimation of the economic impact of vaccination via chosen variables is clearly stated in [Table/Fig-3].

The results for the sensitivity analysis conducted in this study are shown in [Table/Fig 4] and [Table/Fig 5].

	Total Cost	QALY lost due to having influenza	Cost/QALY (ICER)
<b>Social perspective</b>			
Get influenza vaccine	37.427	0.017	20.118
No influenza vaccine	17.994	0.983	
<b>Healthcare perspective</b>			
Get influenza vaccine	18.326	0.017	15.967
No influenza vaccine	2.902	0.983	

[Table/Fig-3]: Incremental Cost-Effectiveness Ratios of influenza vaccination versus no influenza vaccination in children under 15-year-old.

As with the social perspective, the expected total cost will not show any differences, whereas the ICER value will change  $\pm 0.35\%$  if the QALY gained due to influenza symptoms changes by  $\pm 10\%$  [Table/Fig-6].

If the vaccine efficacy is 100% and the influenza virus strain match is 0%, the cost of vaccination will be lowest (25.95 USD) in the social perspective, whereas it will be highest, at 36.45 USD, when the vaccine efficacy and strain match are 20% and 80%, respectively [Table/Fig-7].

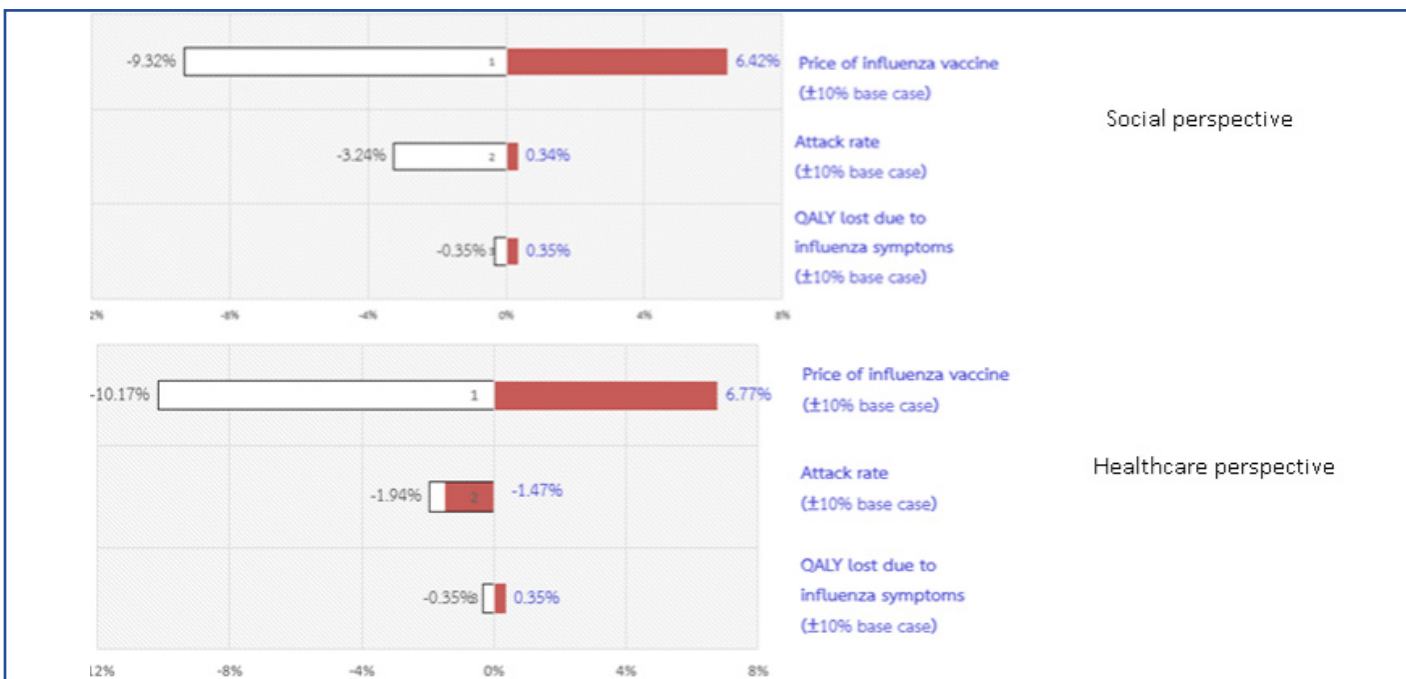
A comparison of the two perspectives indicates that the cost of vaccination and the cost of QALY gained due to influenza symptoms are likely to fluctuate in the healthcare as well as the social perspective. The results indicate that vaccination of children under 15-year-old would not only produce health benefits but it would also provide cost savings from the healthcare provider perspective. Cost savings or cost benefits were vulnerable to the incidence of disease [Table/Fig-8]. As shown in [Table/Fig-9], the results of cost benefit value from the healthcare provider perspective were 38.7 million USD at 97.2% vaccination coverage. The same as for the whole cohort of vaccinated children [28] [Table/Fig-10].

## DISCUSSION

In this study, the ICER of influenza vaccination versus no influenza vaccination in children under 15-year-old was 25.31 USD/QALY

Variables	Social Perspective						Healthcare Perspective					
	Change	Expected total cost	Percent change	Cost/QALY gained	Percent change	Change	Expected total cost	Percent change	Cost / QALY gained	Percent change		
Price of influenza vaccine	(-10%)	25.16	28.40	-6.35%	22.95	-9.32%	14.86	19.23	-6.61%	27.87	-10.17%	
	Base case	26.00	30.32	-	25.31	-	16.51	20.60	-	31.03	-	
	(+10%)	27.20	32.25	6.35%	26.94	6.42%	18.16	21.96	6.61%	33.12	6.77%	
Attack rate	(-10%)	0.09	29.89	-1.44%	24.49	-3.24%	0.09	20.53	-0.34%	30.42	-1.94%	
	Base case	0.10	30.32	-	25.31	-	0.10	20.60	-	31.03	-	
	(+10%)	0.11	30.76	1.44%	25.40	0.34%	0.11	20.67	0.34%	30.57	-1.47%	
QALY gained due to influenza symptoms	(-10%)	0.015	30.32	0.00%	25.22	-0.35%	0.015	20.60	0.00%	30.92	-0.35%	
	Base case	0.017	30.32	-	25.31	-	0.017	20.60	-	31.03	-	
	(+10%)	0.019	30.32	0.00%	25.40	0.35%	0.019	20.60	0.00%	31.14	0.35%	

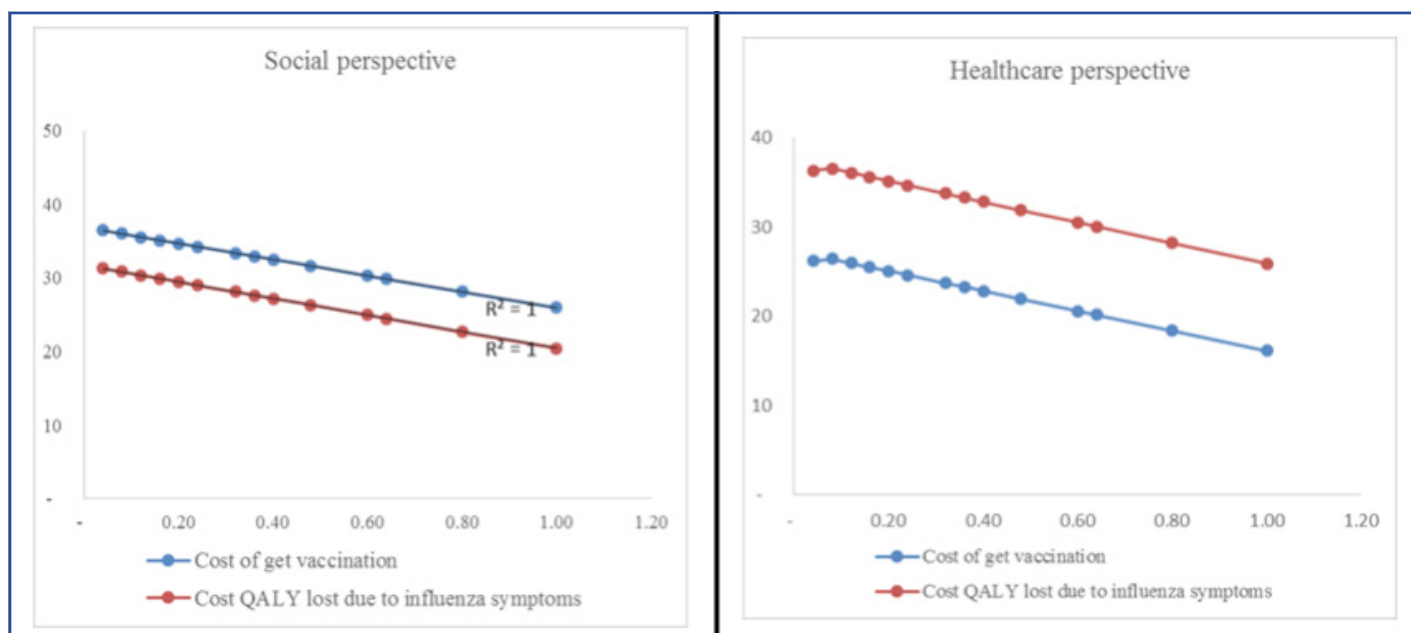
[Table/Fig-4]: Sensitivity analysis of the main variables that may affect the results.



[Table/Fig-5]: Tornado diagram.

	Strain match	Social perspective					Healthcare perspective						
		0.00	0.20	0.40	0.60	0.80	0.00	0.20	0.40	0.60	0.80		
Cost of vaccination	Vaccine efficacy	0.2	34.70	35.13	35.57	36.01	36.45	0.2	25.06	25.51	25.95	26.40	26.20
		0.4	32.51	33.39	34.26	35.13	36.01	0.4	22.83	23.72	24.61	25.51	25.12
		0.6	30.32	31.64	32.95	34.26	35.57	0.6	20.60	21.94	23.27	24.61	24.03
		0.8	28.14	29.89	31.64	33.39	35.13	0.8	18.36	20.15	21.94	23.72	22.94
		1.0	25.95	28.14	30.32	32.51	34.70	1.0	16.13	18.36	20.60	22.83	21.85
Cost QALY lost due to influenza symptoms	Vaccine efficacy	0.2	29.47	29.92	30.38	30.83	31.28	0.2	35.12	35.58	36.04	36.51	36.30
		0.4	27.21	28.11	29.02	29.92	30.83	0.4	32.81	33.73	34.66	35.58	35.18
		0.6	24.95	26.30	27.66	29.02	30.38	0.6	30.50	31.88	33.27	34.66	34.05
		0.8	22.68	24.49	26.30	28.11	29.92	0.8	28.19	30.04	31.88	33.73	32.92
		1.0	20.42	22.68	24.95	27.21	29.47	1.0	25.88	28.19	30.50	32.81	31.80

[Table/Fig-6]: Costs and outcomes for with changes in vaccine efficacy and strain mismatch.



[Table/Fig-7]: Cost of vaccination and cost of QALY lost due to influenza symptoms with changes in effective vaccination.

and 31.03 USD/QALY for the social and healthcare provider perspectives, respectively. In Vietnam, there is no Willingness-To-Pay (WTP) threshold, so it is difficult to compare the Vietnamese situation with WTP to evaluate vaccination effectiveness.

However, according to the WHO, WTP can be calculated based on the GDP. The GDP of Vietnam in 2016 was 2,100 USD [29], which indicates that vaccination was economically efficient relative to no vaccination.

	Vaccination				No Vaccination
	90.0	95.0	97.2	100.0	
Vaccine coverage (%)	90.0	95.0	97.2	100.0	
Population	19,800,000	20,900,000	21,384,000	22,000,000	22,000,000
Immunized children (% Vaccine Efficacy)	11,880,000	12,540,000	12,830,000	13,200,000	-
Total cost of vaccination	83,397,600	88,030,800	90,069,408	92,664,000	-
Number of influenza cases	792,000	836,000	855,360	880,000	3,520,000
Cost of treatment	320,823,360	338,646,880	346,489,229	356,470,400	396,281,600
<b>Cost treatment saving</b>	<b>-75,458,240</b>	<b>-57,634,720</b>	<b>-49,792,371</b>	<b>-39,811,200</b>	-
<b>Net benefit value</b>	<b>-35,830,080</b>	<b>-37,820,640</b>	<b>-38,696,486</b>	<b>-39,811,200</b>	-

**[Table/Fig-8]:** Cost saving of vaccination versus no vaccination in children under 15 years old (USD).

Vaccine coverage	0%	10.0%	20.0%	30.0%	40.0%	50.0%	60.0%
No. of children prevented by vaccination	-	2,200,000	4,400,000	6,600,000	8,800,000	11,000,000	13,200,000
Illness cases	3,520,000	3,256,000	2,992,000	2,728,000	2,464,000	2,200,000	1,936,000
Cost benefit of Healthcare perspective (USD) when comparing to non-coverage vaccine	-	-3,981,120	-7,962,240	-11,943,360	-15,924,480	-19,905,600	-23,886,720
Vaccine coverage	70.0%	80.0%	85.0%	90.0%	95.0%	97.2%	100.0%
No. of children prevented by vaccination	15,400,000	17,600,000	18,700,000	19,800,000	20,900,000	21,384,000	22,000,000
Illness cases	1,672,000	1,408,000	1,276,000	1,144,000	1,012,000	953,920	880,000
Cost benefit of Healthcare perspective (USD) when comparing to non-coverage vaccine	-27,867,840	-31,848,960	-33,839,520	-35,830,080	-37,820,640	-38,696,486	-39,811,200

**[Table/Fig-9]:** Cost benefit analysis for an influenza vaccination program in children under age 15.

Notes: Cost benefit of Healthcare perspective <0: Cost-saving. Cost benefit of Healthcare perspective >0: Non cost-saving

	Influenza vaccination for children	Scenario 1. Children under one-year-old	Scenario 1. Children under six-year-old	Scenario 2. Children under 15-year-old
For the first year	The number of doses is estimated to supply	1,996,052	12,150,000	29,700,000
	Total vaccine cost (USD)	20,419,611	124,294,500	303,831,000
For subsequent years	The number of doses is estimated to supply	1,396,842	9,520,000	23,560,000
	Total vaccine cost (USD)	14,289,689	97,389,600	241,018,800

**[Table/Fig-10]:** Comparison of budget impact analysis to cover influenza vaccination for children under one, six and 15-year-old.

In other countries, such as Italy, from the perspective of the Italian healthcare service, influenza vaccination of 6- to 60-month-old and 6- to 24-month-old children cost 10,000 Euros and 13,333 Euros per QALY saved, respectively [10]. In the US, the cost per QALY was 216.25 USD for children from 24 to 59-month-old who received TIV [10]. The US study estimated that the ICER for using an inactivated influenza vaccination for children not at high risk were 28,000 USD per QALY, 79,000 USD per QALY and 119,000 USD per QALY for children with 3 to 4-year-old, 5 to 11-year-old and 12 to 17-year-old [30].

Our costs and ICER estimates were lower than estimates from middle- or other high-income countries [4] because the healthcare system in Vietnam is radically different. The diagnostic tests and routine procedures common in middle- and high-income countries for patients with ILI are infrequently practiced in Vietnam. For instance, only 2 health facilities in southern Vietnam can confirm influenza based on Polymerase Chain Reaction (PCR).

These results presented here agreed with those of other studies [13,31]. Studies in Spain and Argentina had a lesser mean cost of disease among children who were vaccinated.

The study in Argentina indicated that general influenza vaccination for children under age 15 would result in substantial cost savings for society, at 11.9 million USD, when compared with a non-interference program [13].

## LIMITATION

This study has some limitations. On the one hand, due to the possible inaccuracy and instability of the chosen statistics, the results are unlikely to be a genuine and reliable source of data. Thus, parameters cannot be obtained for the Vietnamese population. For instance, influenza-related complications could develop in many cases of hospitalised children. On the other hand, the direct medical costs and the number of influenza-related hospitalisations, particularly for patients with influenza diagnosed as a secondary disease, are subject to the greatest potential for medical errors.

The records of health care used for influenza vaccination and the infection rate in households were not collected at the time of the trial, so other sources of literature were used to evaluate costs and resources. The economic analysis therefore shows slight signs of bias towards prevention due to the excluded external benefits. Furthermore, natural immunity was known to take effect at a maximum timespan of ten years; however, due to the nature of antigenic variation, this immunity may not sustain protection against new virus variants.

A high rate of coverage would afford external benefits to those who were unvaccinated, as they would not contract the illness from those who had been vaccinated and perhaps could afford some level of protection to those outside of Hong Kong. Hence, the true benefits derived from a vaccination program could be greater than stated in the economic analysis.

In 2016, the total budget to cover VEPI was 29.98 million USD. The results of the BIA indicate the total budgets for children under one-year-old, six-year-old, and 15-year-old for the first year is 20.42, 121.29, and 303.81 million USD, respectively. When comparing the budget to cover VEPI, the healthcare provider should be considered for children under one-year-old.

## CONCLUSION

The development of vaccination policies is a challenge for policy makers who must take the willingness of society to pay for specific illness prevention and outcomes into consideration. From the viewpoint of either healthcare or society, influenza vaccination is an expensive, yet effective, intervention for children under 15 years of age. Decision-makers could be coaxed with the information from this study that vaccination is the best intervention for the

control of influenza in children at high risk. Hence, the demand continues for further and more detailed research that concentrates mainly on evaluating the burden of influenza to justify the benefits of vaccination in a more impartial and explicit manner. Economic and mathematical models are needed to better inform the policy decisions regarding influenza prevention and control and to direct influenza vaccination into VEPI.

## ABBREVIATIONS

ICER=Incremental Cost-Effectiveness Ratio; ILI=Influenza-Like Illness; IPD=Inpatient Department; LCI=Laboratory Polymerase Chain Reaction-Confirmed Test; OPD=Outpatient Department; QALY=Quality-Adjusted Life-Years; TIV=Trivalent Inactivated Influenza Vaccine; USD= the United State Dollar; VEPI=Vietnamese Expanded Program On Immunisation.

## DISCLOSURE

The Authors declare that they have no relevant conflicts of interest to disclose.

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